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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/551,977	04/14/00	POLO J	930049.489/1

027476
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HM12/1002

EXAMINER	
LI, B	
ART UNIT	**PAPER NUMBER**
1648	13

DATE MAILED: 10/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

PTO-90C (Rev. 2/95)

1- File Copy

*U.S. GPO: 2000-473-000/44602

Office Action Summary	Application No.	Applicant(s)	
	09/551,977	POLO ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *1-16,18 and 24-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17 and 19-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *72/1 &8* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Claims 1-37 are pending.

Election/Restrictions

Applicant's election with traverse of Group V, claims 17 and 19-23 in Paper No. 10 is acknowledged. The traversal is on the ground(s) that the searching more than one groups restricted by the previous office action can reduce the burden of the examiner's search. This is not found persuasive because different groups of the inventions as restricted by the previous office action are directed to either structurally and/or functionally different distinct inventions. A complete searching both in house and in commercial database for different inventions will constitute a serious burden for the office.

The requirement is still deemed proper and is therefore made FINAL.

Applicants are required to cancel all non-elected claims 1-16, 18, 24-37 to the non-elected groups.

Applicant is also reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims 17 and 19-23 are considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 is vague in that the metes and bonds of the recombinant alphavirus particle are not defined. However, since most alphavirus are not recognized to be able to infect human dendritic cells (DC), and however, there are so many alphaviruses in the art, the claim should point out which alphavirus is intended in the said claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17 and 21-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for having a recombinant Sindbis virus, which is capable to infect the human DC, by substation of Gly for Glu at residue 160 of said Sindbis virus , does not reasonably provide enablement for having any or all recombinant alphavirus being capable infecting human DC . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and gain in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988). These factors include the following:

1). Unpredictability of the art. The initial target cells for the alphavirus infection is not clear and whether any or all recombinant aphaviruses can infect human DC is unpredictable. Some point mutation may accidentally be able to abolish the infective ability of an alphavirus for human DC. For example, McDonald et al. (J. Virol. 2000, Vol. 74, pp. 914-922) reported that a recombinant aphavirus Venezuelan Equine Encephalitis vector carrying a green flourescece protein can infect DC, however, a substitution mutation from Glu to Lys at the residue 76 totally abolish the ability for the said virus to infect DC, whereas an mutation of Lys to Glu at the residue 116 of E2 restore the ability for infecting DC (see entire document).

2) State of the art. The initial target cell for the alphavirus infection is poorly understood. The art at has demonstrated that mutation at the E2 region of alphavirus can alter the virus

neurovirulence and viral entry into the cells as evidenced by Tucker et al. (J. Virol. 1997, Vol. 71, pp. 6106-6112, see entire document) and McDonald et al. described supra (J. Virol. 2000, Vol. 74, pp. 914-922, see entire document). Polo's group, an inventor of instant application, (Gardner et al. J. Virol. Dec. 2000, Vol. 74, pp. 11849-11857) reports that a Sindbit virus with a substitution mutation of Gly to Glu at the residue 160 of E2 region can infect human DC. However, they concluded that the level of the toxicity of the mutated Sindbits virus to the primary human DC unfortunately prevent them to do further investigation (see entire document).

3) Number of working examples. Applicants present no working examples of any other alphavirus except a recombinant Sindbit virus with a substitution mutation of Gly to Glu at the residue 160 of E2 region can infect human DC.

4) Amount of guidance presented in the specification. Applicants present no guidance on how the skilled artisan would practice successfully with any or all recombinant alphavirus vector can infect human DC.

5) Scope of the claims. The claims broadly read on a recombinant alphavirus can infect human DC.

6) Nature of the invention. The invention involves a complex and unpredictable field.

7) Lever of the skill in the art. The requirement of level of the skill for constructing a recombinant alphavirus vector with an ability to infect human DC is high. Without proper guidance, a large quantity of non-routine experiment has to be conduct for constructing and selecting an recombinant alphavirus being ca[able to infect the human DC.

Given the above analysis of the factors, which the courts have determined, are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan would have had to conduct undue and excessive experimentation in order to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 17, 19 and 21-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Song et al. (WO 97/24447).

Song et al. teach a recombinant aphavirus that can target human dendritic cells (see claims 1-4). Therefore, the claimed invention is anticipated by the cited prior art.

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 17, 19 and 21-23 are rejected under 35 U.S.C. 102(a) as being anticipated by Bungener et al. (J. Leukocyte biology Oct. 1998, supp. [2], pp. K2-K2).

Bungener et al. teach to use recombinant alphavirus, Semliki Forest virus, to infect human and murine dendritic cells. Therefore, the claimed invention is anticipated by the cited reference. (see entire document). Therefore, the claimed invention is anticipated by the cited prior art.

Claim Rejections - 35 USC § 103

Claim 20 is deemed free of prior art, given failure of the prior art to teach or reasonably suggest that a recombinant Sindbits virus with substitution mutation from Gly to Glu at the residue 160 of E2 region can be able to infect human DC. The closest art taught by Klimstra et al (J. Virol. 1998, Vol. 72, pp. 7357-7366) or Tunker et al. (J. Virol. 1997, Vol. 71, pp. 6106-6112) teach that some substitutive mutation of a single amino acid located at the different position of E2 region, which can increase the binding ability of the Sindbits virus to baby hamster kidney cells (BHK) or change the virulence. However, there is no indication that any mutation at the E2 region can enable Sindbits virus infect human DC.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 8:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li

September 27, 2001

ALI R. SALIMI
PRIMARY EXAMINER